Appl. No. 10/677,641 Amdt. dated February 4, 2004 Reply to Notice to File Missing Parts of January 22, 2004

Amendments to the Specification:

Please replace paragraph [01] beginning at page 1, line 9, with the following:

--[01] This application claims priority to International Application no. PCT/______No. PCT/US03/10384, which was filed on April 1, 2003, which application claims the benefit of Provisional Application Serial No. 60/369,741 filed April 1, 2002, Provisional Application Serial No. 60/379,688 filed May 9, 2002 and Provisional Application Serial No. 60/425,719 filed November 12, 2002, all of which are incorporated hereby by reference.--

Please replace paragraph [78] beginning at page 25, line 14, with the following:

--[78] Particularly preferred fusion proteins include amino acid sequences that facilitate purification or identification of the fusion protein. Exemplary amino acid sequences of this type include affinity tags and secretory sequences. Other tags or labels are also known in the art and applicable to the present invention. Common fusion protein sequences of this type include glutathione S-transferase ("GST"), thioredoxin ("Trx"), maltose binding protein, C- and/or N-terminal hexahistidine (SEQ ID NO:10) polypeptide (His tag), polylysine and other binding molecules. Other embodiments are coupled to elements that allow the fusion proteins to be easily identified, such as small fluorescent proteins, antigenic determinants(e.g., FLAG, CD4, HA), enzymes that produce detectable products and the like. Still other embodiments are coupled to signal elements that direct the target products to particular cellular compartments. Examples of signal elements include those directing proteins to cellular organelles or identify the protein for excretion, the secretory signal segments.--

Appl. No. 10/677,641 Amdt. dated February 4, 2004 Reply to Notice to File Missing Parts of January 22, 2004

Please replace paragraph [107] beginning at page 35, line 16, with the following:

--[107] Proteins expressed using the translationally-harmonized nucleic acids of the present invention may be isolated from the translation systems used to express them using any technique, or combination of techniques, known to those of skill in the art. Suitable techniques include selective precipitation with such substances as ammonium sulfate; column chromatography using conventional matrices or those substituted with ligands (e.g., nickel-substituted nitroloacetic acid) that interact with encoded "affinity tags" (e.g., hexa histidine (SEQ ID NO:10) tags), immunopurification methods, and others (see, e.g., Scopes, Protein Purification: Principles and Practice (1982); U.S. Patent No. 4,673,641; Ausubel et al., supra; and Sambrook et al., supra). A number of procedures can be employed to purify expressed fusion proteins of the invention. For example, expressed fusion proteins may be purified using immunoaffinity columns, or from growth-conditioned cell culture medium by immunoaffinity and ion exchange chromatography as described in Leonard et al., J. Biol. Chem. 265:10373-10382 (1990).--

Please replace paragraph [130] beginning at page 44, line 10, with the following:

--[130] In a studies design to produce a potentially important malarial antigen, we found that the levels of soluble MSP1-42 (FVO) protein obtained following induction of BL21 DE3 cells expressing the wild type gene sequence, pET(AT)FVO were negligible and insufficient to advance for further process development. Rather than changing to a new expression system, such a Pichia, or baculovirus, we chose to try to overcome this problem owing to the advantages that E. coli offers, especially with respect to expression of non-glycosylated protein. Our initial thinking was that it might be important to preserve ribosomal pausing (i.e., attenuate translation) at certain times to allow for protein folding. We thought that we might achieve this by analyzing the target gene to reveal clusters of low abundance codons and changing those codons if necessary ("harmonizing") so that they would correspond to codons of low abundance in the expression host (in this case *E. coli*). For the first approach to codon harmonization, we used, as

Appl. No. 10/677,641 Amdt. dated February 4, 2004 Reply to Notice to File Missing Parts of January 22, 2004

reference materials, codon frequency tables for P. falciparum (Saul A & Battistutta D. Codon usage in Plasmodium falciparum. Mol Biochem Parasitol 1988; 27:35-42.) and E. coli (Data Reference Set, Volume 3: Data Files, Genetics Computer Group, Sequence Analysis Software Package). The entire codon usage data set for both organisms is presented in table 1 Table 1 (AA = SEQ ID NO:8; Native codon = SEQ ID NO:7; Harmonized codon = SEQ ID NO:9). We evaluated consecutive codons as rolling triplets along the range of amino acids of interest, paying special attention to the patterns associated with domain segments, which separate minimal domain structures, i.e. alpha helices, beta pleated sheets. Within interdomain segments, the amino acid content is restricted to about half of the common amino acids and their corresponding codons tend to be used infrequently, indicating that translation proceeds slowly in these regions. This slowdown in translation within interdomain segments may allow nascent protein to complete the folding of one domain prior to initiating synthesis of the next.--

Please cancel the present informal "SEQUENCE LISTING", page 59, and insert therefor the accompanying paper copy of the formal Sequence Listing, page numbers 1 to 6, at the end of the application. Cancel the page numbers for Table 1, pages 60-66, and renumber as pages 59-65, accordingly.